The attached Appendix includes marked-up copies of each rewritten claim (37 C.F.R. §1.121(c)(1)(ii)).

35 U.S.C. §112 Rejections

Claims 22-42 are rejected under 35 U.S.C. §112, second paragraph. The Office Action asserts that claims 22-42 are indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. Applicants respectfully traverse the rejection.

Claims 22, 28, 39 and 40 are rejected based on improper claim language. M.P.E.P. §2173.05(d). By this Amendment, claims 22, 28, 39 and 40 are amended to remove the improper claim language.

Regarding claims 22-42, the Office Action asserts that the phrase "X represents a group which limits the diffusion of the alpha-keto acid produced by the deamination of the cyclic amino acid" is unclear. The Office Action further asserts that the chemical group "X" as claimed is indefinite and that the specific chemical groups to which "X" is directed are unclear.

The importance of detecting and identifying microorganisms is known. It is common for persons of ordinary skill in the art to assay enzymatic activity when detecting and identifying microorganisms. In these assays, molecules are introduced to a cell and are hydrolyzed, in the presence of a specific enzyme, and subsequently release a colored or fluorescent compound.

Diffusion of the colored/fluorescent compound is a known problem associated with these assays. Page 3, lines 8-13. For example, diffusion of the colored/fluorescent compound may interfere with the detection of other microorganisms. Page 7, lines 1-2. Two known causes of this diffusion are 1) substrate hydrolysis in a wide zone around the colony and further diffusion of the colored product; and 2) export of the colored product out of the cell

and subsequent diffusion of the product. A solution proposed by the prior art for limiting the diffusion of an α-keto acid produced by the deamination of the cyclic amino acid is to limit the incubation time. However, this will prejudice the quality of the detection. Page 4, lines 16-19.

Although the claims do not identify specific chemical groups for X, Applicants submit that one of ordinary skill in the art would understand what chemical groups can be substituted on a cyclic amino acid radical. The present specification discloses examples that do not limit the scope of the claims. Page 11 and Examples 1-9. Further, the present specification discloses a simple method for determining whether or not a potential X chemical group limits diffusion of the α-keto acid in culture medium produced by the deamination of the cyclic amino acid. Page 5, line 33 to page 6, line 7.

all chemical group which can be substituted on a cyclic amino acid radical are potential X groups?

Regarding claims 22 and 30, the Office Action asserts that it is unclear where and how the diffusion is limited. By this Amendment, claims 22 and 30 are amended to clearly define that diffusion of the alpha-keto acid is limited in culture medium.

One of ordinary skill in the art would understand that, according to the claimed invention, diffusion of the α-keto acid in culture medium is limited either by interactions of hydrophobic group(s) with hydrophilic medium, or by interactions of chemical group(s) with cell constituents. Further, one of ordinary skill in the art would understand that this limiting of the diffusion of the α-keto acid in culture medium improves the assay by preventing interference with the detection of other microorganisms and by preventing a weakening of the color/fluorescence signal. Page 7, lines 1-2.

Regarding claims 23 and 31, the Office Action asserts that the limitation "hydrophobic groups" is unclear and too broad. The group "X" is limited to include only those chemicals that limit the diffusion of an alpha-keto acid. It would be clear to persons of ordinary skill in

the art that hydrophobic chemical groups are nonpolar and are insoluble in water. The limitation "hydrophobic" serves to further limit "X," in that "X" must be a hydrophobic chemical group that limits the diffusion of an alpha-keto acid.

Regarding claim 25, the Office Action asserts that the term "cation salt" is indefinite and broad. Applicants respectfully traverse this rejection. Cation salts are commonly used as revealing agents in enzyme activity assays. Persons with ordinary skill in the art would know which cation salts are appropriate for use as revealing agents. This fact is supported by at least the following references: U.S. Patent 5,643,743, U.S. Patent 5,411,867, U.S. Patent 5,541,082, U.S. Patent 4,603,108 and International Patent Application WO 92/00068, all of which have been made of record. The specification highlights specific examples of cation salts that do not limit the claims. Examples 1-9.

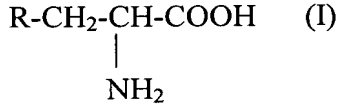
okay

For at least the reasons discussed above, Applicants respectfully submit that one of ordinary skill in the art would be readily able to understand the scope and meaning of the claims. Accordingly, all of claims 22-42 satisfy the requirements of 35 U.S.C. §112, second paragraph. Reconsideration and withdrawal of the rejection are respectfully requested.

35 U.S.C. §102 Rejection

Claims 30 and 31 are rejected under 35 U.S.C. §102(b) as being anticipated by each of Voelter ('352), Tam et al. ('230), Deghengi ('254) and Morris et al. ('434). Applicants respectfully traverse the rejection.

Independent claim 30 is directed to a compound having the general formula (I):



(I)

in which:

- R represents a cyclic amino acid radical, substituted with 2 or 3 groups X, which are identical or different,

X represents a group which limits the diffusion in the culture medium of the α-keto acid produced by the deamination of the cyclic amino acid.

Voelter discloses a process for the preparation of new N^{τ}-substituted histidine derivatives, examples of which include: 3-propylhistidine, 3-isopropylhistidine, 3-butylhistidine, 3-cyclopropylhistidine, 3-cyclopentylhistidine and 3-benzylhistidine. Column 11, lines 25-33.

Tam discloses a method of releasing a functional group present in an amino acid or amino acyl residue from a resin or protecting residue, which is bonded to the functional group by a linkage having proton affinity. A side-product of the deprotection of Boc-Tyr (Bzl) by an S_N1 reaction is 3-benzyl-tyrosine. Column 11, line 3.

Deghengi discloses D-2-alkylTryptophan and peptides containing D-2-alkylTryptophan. Homologous alkylated derivatives can be prepared from 2-methyl-Tryptophan. Column 4, lines 37-39.

Morris discloses a process for measuring fluorescence that uses p-nitro-phenylalanine. Column 13, line 11.

None of the cited references teaches each and every element of claim 30. Specifically, each of the cited references discloses a single chemical group on a cyclic amino acid. None of the cited references teach a compound in which a cyclic amino acid radical is substituted with two or three chemical groups. Accordingly, claim 30 is not anticipated by any of the cited references.

Claim 31 depends from claim 30. Accordingly, dependent claim 31 is not anticipated by any of the cited references, for at least the reasons discussed above. Reconsideration and withdrawal of the rejection are respectfully requested.

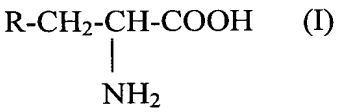
35 U.S.C. §103 Rejection

Claims 22-23, 25-29 and 36-42 are rejected under 35 U.S.C. §103(a) as being unpatentable over Morris in view of Sellers ('203). Applicants respectfully traverse the rejection.

The compound of claim 30 is discussed above. Claim 36 is directed to a method for preparing the compound of claim 30, and claims 37-42 are directed to a culture medium that comprises the compound of claim 30. Neither Morris, as discussed above, nor Sellers teach or suggest the compound of claim 30. Specifically, neither Morris nor Sellers teach or suggest a compound in which a cyclic amino acid radical is substituted with 2 or 3 groups X, which are identical or different.

Claims 22, 23 and 25-29 are directed to a method for detecting and identifying and/or quantifying an enzymatic activity of a microorganism wherein a microorganism with a deaminase activity is brought into contact with a culture medium comprising at least one detection agent for demonstrating, by forming a colored product with a revealing agent, an enzymatic activity;

said detection agent being an L-amino acid of following general formula (I):



(I)

in which R represents a cyclic amino acid radical, substituted with 1 to 3 groups X, which are identical or different, and X represents a group which limits the diffusion in the culture medium of the α-keto acid produced by the deamination of the cyclic amino acid.

As discussed above, Morris discloses a process for measuring fluorescence that uses p-nitro-phenylalanine. As indicated in the Office Action, Morris does not disclose that the amino acid detecting agent is present in the culture medium. In addition, Morris does not

teach or suggest an X group that limits diffusion, in a culture medium, of the α-keto acid produced. In contrast, Morris discloses a modified amino acid in which the amino acid is substituted by a NO_2 group. NO_2 confers hydrophilic properties to the reaction product and thus promotes diffusion. Thus, Morris, in fact, teaches away from the claimed invention.

Sellers does not overcome the deficiency of Morris. Specifically, Sellers does not teach or suggest a method in which an amino acid radical of a detecting agent is substituted with any chemical group, much less chemical group(s) that limit the diffusion of an α-keto acid.

For at least these reasons, Applicants submit that claims 22-23, 25-29 and 36-42 are patentable over the cited references. Reconsideration and withdrawal of the rejection are respectfully requested.

I. New Claims

New claims 43-44 and 45-46 ultimately depend from claims 22 and 30, respectively. For at least the reasons stated above, new dependent claims 43-46 are patentable over the cited references.

New claim 47 is directed to a compound in which R is substituted by one group X, and X represents 1) any hydrophobic group that limits the diffusion of the alpha-keto acid in a hydrophilic medium or 2) any group, which makes it possible to bind to cell constituents. The compound may not be N-im-benzyl-L-histidine, 1- and 3-methyl-L-histidine, o-benzyl-L-tyrosine, o-carboxybenzoyl-L-tyrosine, o-dansyl-L-tyrosine, o-methyl-L-tyrosine and 1-, 4-, 5-, 6- and 7-methyl-L-tryptophan.

None of the cited references teach or suggest the claimed compound in which X represents 1) any hydrophobic group that limits the diffusion of the alpha-keto acid in a hydrophilic medium or 2) any group which makes it possible to bind to cell constituents. For at least these reasons, Applicants submit that claim 47 is patentable over the cited references.

Conclusion

In view of the above amendments and remarks, it is respectfully submitted that the present application is in condition for allowance. Favorable consideration and prompt allowance are therefore respectfully requested.

Should the Examiner believe that anything further would be desirable in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below.

Respectfully submitted,

William P. Berridge
Registration No. 30,024

Melanie L. Mealy
Registration No. 40,085

WPB:PAC/jca

Attachment:
Appendix

Date: January 23, 2002

OLIFF & BERRIDGE, PLC
P.O. Box 19928
Alexandria, Virginia 22320
Telephone: (703) 836-6400

DEPOSIT ACCOUNT USE AUTHORIZATION
Please grant any extension necessary for entry;
Charge any fee due to our Deposit Account No. 15-0461

APPENDIX

Changes to Claims:

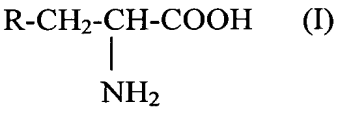
Claims 43-47 are added.

The following are marked-up versions of the amended claims:

22. (Amended) Method for detecting and identifying and/or quantifying an enzymatic activity ~~such as deaminase activity~~ of a microorganism, according to which an inoculum which is capable of containing a microorganism with a deaminase activity is brought into contact with a culture medium for microorganisms,

~~characterized in that~~wherein the culture medium comprises at least one detection agent for demonstrating, by forming a colored product with a revealing agent, an enzymatic activity ~~such as deaminase activity~~;

said detection agent being an L-amino acid of following general formula (I):



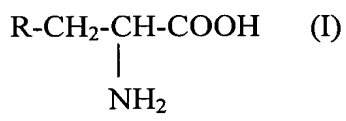
(I)

in which:

- R represents a cyclic amino acid radical, substituted with 1 to 3 groups X, which are identical or different,
- X represents a group which limits the diffusion in the culture medium of the α-keto acid produced by the deamination of the cyclic amino acid.

28. (Amended) Method according to claim 22, ~~characterized in that~~wherein the microorganisms which are detected and identified and/or quantified by enzymatic activity ~~such as deaminase activity~~ belong to the group *Proteus*.

30. (Amended) Compound having the following general formula (I):



(I)

in which:

- R represents a cyclic amino acid radical, substituted with ~~1 to~~2 or 3 groups X, which are identical or different,

- X represents a group which limits the diffusion in the culture medium of the α-keto acid produced by the deamination of the cyclic amino acid~~,~~

~~with the exception of the compounds N-im-benzyl-L-histidine, 1- and 3-methyl-L-histidine, o-benzyl-L-tyrosine, o-carboxybenzoyl-L-tyrosine, o-dansyl-L-tyrosine, o-methyl-L-tyrosine and 1-, 4-, 5-, 6- and 7-methyl-L-tryptophan~~.

39. (Amended) Culture medium according to claim 37, ~~characterized in that~~wherein weight concentration of the detection agent(s) is between 0.1 and 2 g/l~~, preferably between 0.3 and 0.6 g/l~~.

40. (Amended) Culture medium according to claim 37, ~~characterized in that it also comprises~~further comprising a revealing agent~~, preferably a cation salt, for example ammoniacal iron citrate~~.